Remarks

No new matter has been added as a result of the above amendments.

Rejection of claims 1, 2, 4, 6-12, 14, 16-21, 23, 25-31, 33 and 35-38 are rejected under 35 USC 112, ¶1

Claims 1, 2, 4, 6-12, 14, 16-21, 23, 25-31, 33 and 35-38 are rejected under 35 USC 112, ¶1. Applicant respectfully disagrees.

The Examine states that "while being enabling [referring to the present specification] for the compounds of amlodipine, amlodipine besylate, atorvastatin and the hemicalcium salt of atorvastatin, [it] does not reasonably provide enablement for other types of derivatives ..." The Examiner goes to say that [*sic*] "[t]he prior art, Buch of U.S. Patent No. teaches of various types of pharmaceutically acceptable salts for the compounds of amlodipine and atorvastatin ..."

It is a basic tenant of patent law that the scope of a claim is viewed in light of the prior art. Here, Applicant is claiming "effective derivatives of" either amlodipine or atorvastatin, (depending upon the specific dependent claim). The derivatives of both of these drugs are not only found in Applicant's specification, but also in the prior art, *e.g.*, Buch's '574 US patent. Applicant's dependent claims (which claim effective derivatives of either amlodipine or atorvastatin) should be read in view of the current specification as well as what is public knowledge. The present invention does not lie with the derivatives themselves, rather in the synergistic effect resulting therefrom. The Applicant is not claiming the derivatives for themselves, rather in the ability to produce a synergistic effect.

Moreover, it is axiomatic in patent law that any claim depending from an independent claim that claims allowable subject matter also defines allowable subject matter. (See *In re* Fine, 837 F.2d 1071, 1076, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988.) The derivative claims are depending from claims that, in the view of the Applicant,

define allowable subject matter. Therefore, Applicant contends that the dependent claims claiming derivatives also define allowable subject matter.

Applicant respectfully requests reconsideration and withdrawal of the present rejection.

Rejection of claims 1-8, and 20-27 are rejected under 35 USC 102(e)

Claims 1-8 and 20-27 are rejected under 35 USC 102(e) as being anticipated by Buch (US 6,455,574). Applicant respectfully disagrees.

The Examiner states that Buch [*sic*] "disclose of pharmaceutical compositions that contain atorvastatin or its pharmaceutically acceptable salt ... and amlodipine along with its pharmaceutically acceptable salts, ... In addition, Buch teach of utilizing these pharmaceuticals for treating angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia as well as patients with symptoms of cardiac risk." *Office Action, pp 5-6.*

Section 102 of Title 35 provides the novelty requirements for patentability. In order for a prior art reference to anticipate a claim it must teach each and every element of that claim. M.P.E.P. §2131. The Court of Appeals for the Federal Circuit states:"[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628 (CAFC, 1987).

Claims 1 through 10 and claims 20 through 29 have been canceled. Moreover, the amended claims of the present invention recite elements not contained in the Buch disclosure. For example, the amended claims include the element of synergistically increasing nitric oxide production. This element is absent from the Buch disclosure. Therefore, Buch fails as an anticipatory reference by failing to recite each and every element as required by the Court of Appeals for the federal Circuit, *supra.* Hence, Applicant respectfully requests reconsideration and withdrawal of the present rejection.

Rejection of claims 1-8 and 20-27 are rejected under 35 USC 102(e)

Claims 1-8 and 20-27 are rejected under 35 USC 102(e) as being anticipated by Chang *et al.* (US 6,262,092). Applicant respectfully disagrees.

The Examiner states that Chang *et al.* [*sic*] "disclose of pharmaceutical compositions that contain atorvastatin or its pharmaceutically acceptable salt, namely the hemicalcium salt of atorvastatin, and amlodipine along with its pharmaceutically acceptable salts, such as amlodipine besylate ... Moreover, Chang teach of utilizing these pharmaceuticals for treating hypertension and hyperlipidemia, atherosclerosis, as well as patients with symptoms of cardiac risk." *Office Action, pg. 9.*

Claims 1 through 10 and claims 20 through 29 have been canceled. Moreover, as with Buch, *supra*, the amended claims of the present invention recite elements not contained in the Chang disclosure. For example, the amended claims include the element of synergistically increasing nitric oxide production. This element is wholly absent from Chang *et al.* Therefore, Chang *et al.* fail as an anticipatory reference by failing to recite each and every element as required by the Court of Appeals for the federal Circuit, *supra.* Hence, Applicant respectfully requests reconsideration and withdrawal of the present rejection.

Rejection of claims 1-38 under 35 USC 103(a)

Claims 1-38 are rejected under 35 USC 103(a) as being unpatentable over Buch (US 6,455,574). Applicant respectfully disagrees.

The Examiner states that Buch [*sic*] "disclose of pharmaceutical compositions that contain atorvastatin or its pharmaceutically acceptable salt ... and amlodipine along with its acceptable salt ... In addition, Buch teach of utilizing these pharmaceuticals for treating angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia as well as patients with symptoms of cardiac risk ... althoug Buch does not specifically teach of inhibiting the crystal formation of cholesterol, it is well known in the art that HMG-CoA reductase inhibitors, in particular atorvastatin, are effective inhibiting HMG-

CoA reductase from catalyzing the rate-limiting step of cholesterol biosynthesis. Additionally, Bush is silent to increase in nitric oxide production by endothelial cells with the administration of the very same claimed compounds. However, in both of these instances, applicant is incorporating a functional recitation of a biochemical process. Accordingly, the skilled artisan would have been most certainly motivated to utilize the teachings of Buch to treat the very same ailments that are claimed by the instant invention. Moreover, it is well within the purview of the skilled artisan to utilize the prior art composition, as taught by Buch, in pharmaceutical preparations, which would inherently perform the functional recitations of inherent biochemical processes that occur with the administration of this previously taught compositions of atorvastatin, and amlodipine."

In order to establish a *prima facie* case of obviousness, "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references) must teach or suggest all of the claim limitations." M.P.E.P. §2143, see also, *In re* Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Buch discloses a pharmaceutical combination of amlodipine and atorvastatin and their respective pharmaceutically acceptable salts. Methods of using this combination are disclosed, specifically methods for treating angina pectoris, atherosclerosis, combined hypertension and hyperlipidemia.

The instant invention claims compositions and methods used to treat arterial and related heart diseases. Specifically, the present invention claims a combination of atorvastatin and amlodipine (along with their pharmaceutically acceptable salts). The instant invention claims the use of these drugs in combination to produce a synergistic effect that includes inhibition of cholesterol crystal formation. As the Examiner adroitly points out, Buch is silent as to teaching the inhibition of cholesterol crystal formation (see

Office Action, pg. 10). Moreover, the presently claimed invention is directed to synergistically increasing nitric oxide production through the combination of atorvastatin and amlodipine. Again, as the Examiner points out (see *Office Action, pg. 10*), Buch is completely silent as to this feature of the instant invention as claimed.

The Examiner, aware of these limitations in Buch, invokes an inherency argument. Essentially, the Examiner contends that these two features, *i.e.*, synergistic inhibition of cholesterol formation and the increase in nitric oxide production, is merely inherent within the function of the pharmaceuticals employed. However, the Court of Appeals for the Federal Circuit is quite clear on this subject when it states: "[t]hat which may be inherent is not necessarily known. Obviousness cannot be predicted on what is unknown." *In re* Newell, 891 F.2d 899, 901, 13 USPQ2d 1248, 1250 (Fed. Cir. 1989). The court in Newell continues, "a retrospective view of inherency is not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular claimed combination." *Ibid.* @ 901, citing Smithkline Diagnostics v. Helena Laboratories Corp., 859 F.2d 878, 886-87, 8 USPQ2d 1468, 1475 (Fed. Cir. 1988).

Applying the standard of the court to the instant situation, it appears obvious that the proposed inherency contention proffered by the Examiner fails and Buch cannot be used as prior art for the purpose of defeating the current claimed invention. Simply, there is absolutely no teaching or motivation provided by Buch to render the present claimed invention obvious. Therefore, Applicant respectfully request and reconsideration of the present rejection.

Rejection of claims 1-38 under 35 USC 103(a)

Claims 1-38 are rejected under 35 USC 103(a) as being unpatentable over Chang *et al.* (US 6,262,092). Applicant respectfully disagrees.

The Examiner states that Chang *et al.* [*sic*] "disclose of pharmaceutical compositions that contain atorvastatin or its pharmaceutically acceptable salt ... and

amlodipine along with its pharmaceutically acceptable salts ... Moreover, Chang teach of utilizing these pharmaceuticals for treating hypertension and hyperlipidemia, atherosclerosis, as well as patients with symptoms of cardiac risk ... Despite the fact that Chang *et al.* do not specifically teach of inhibiting the crystal formation of cholesterol, it is well known in the art that HMG-CoA reductase inhibitors, in particular atorvastatin, are effective inhibiting HMG-CoA reductase from catalyzing the rate-limiting step of cholesterol biosynthesis. Additionally, Chang *et al.* are silent to increase in nitric oxide production by endothelial cells with the administration of the very same claimed compounds. However, in both of these cases, the applicant is attempting to incorporate a functional recitation of an inherent biochemical process. Accordingly, the skilled artisan would have been most certainly motivated to utilize the teachings of Chang *et al.* in order to treat the very same ailments that are claimed by the instant invention. Furthermore, it is well within the level of skill of the artisan to employ the prior art composition, as disclosed by Chang *et al.,* in pharmaceutical preparations that would inherently perform the instantly claimed functional recitations because these biochemical processes that occur with the administration of this previously taught compositions of atorvastatin, and amlodipine, are inherent. Hence, the reference renders the instant invention obvious.

The instant invention claims compositions and methods used to treat arterial and related heart diseases. Specifically, the present invention claims a combination of atorvastatin and amlodipine (along with their pharmaceutically acceptable salts). The instant invention claims the use of these drugs in combination to produce a synergistic effect that includes inhibition of cholesterol crystal formation. As the Examiner adroitly points out, Chang *et al.* is silent as to teaching the inhibition of cholesterol crystal formation (see *Office Action, pg. 11*). Moreover, the presently claimed invention is directed to synergistically increasing nitric oxide production through the combination of atorvastatin and amlodipine. Again, as the Examiner points out (see *Office Action, pg. 11*), Chang *et al.* is completely silent as to this feature of the instant invention as claimed.

The Examiner, aware of these limitations in Chang *et al.*, again invokes the inherency argument. Essentially, the Examiner contends that these two features, *i.e.*,

synergistic inhibition of cholesterol formation and the increase in nitric oxide production, is merely inherent within the function of the pharmaceuticals employed. However, as stated above, the Court of Appeals for the Federal Circuit is quite clear on this subject when it states: "[t]hat which may be inherent is not necessarily known. Obviousness cannot be predicted on what is unknown." *In re* Newell, 891 F.2d 899, 901, 13 USPQ2d 1248, 1250 (Fed. Cir. 1989). The court in Newell continues, "a retrospective view of inherency is not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular claimed combination." *Ibid.* @ 901, citing Smithkline Diagnostics v. Helena Laboratories Corp., 859 F.2d 878, 886-87, 8 USPQ2d 1468, 1475 (Fed. Cir. 1988).

Applying the standard of the court to the instant situation, it appears obvious that the proposed inherency contention proffered by the Examiner fails and Chang *et al.* cannot be used as prior art for the purpose of defeating the current claimed invention. Simply, there is absolutely no teaching or motivation provided by Chang *et al.* to render the present claimed invention obvious. Therefore, Applicant respectfully request and reconsideration of the present rejection.

The Examiner is invited to call the undersigned attorney at (617) 854-4237 should he determine that a telephonic interview would expedite prosecution of this case.

Respectfully submitted,

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